

that are available. If you have requested multiple files, you can specify a corrected file name or you can enter "IGNORE" to continue accessing the remaining file names entered.

=> file reg		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 16:57:32 ON 21 JUN 2007
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STRUCTURE FILE UPDATES: 20 JUN 2007 HIGHEST RN 938114-25-1
DICTIONARY FILE UPDATES: 20 JUN 2007 HIGHEST RN 938114-25-1

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

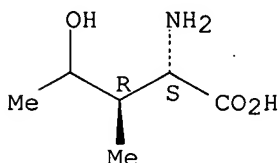
<http://www.cas.org/support/stngen/stndoc/properties.html>

=> s 4-hydroxyisoleucine
19583402 4
5 HYDROXYISOLEUCINE
L1 5 4-HYDROXYISOLEUCINE
(4(W)HYDROXYISOLEUCINE)

=> d 1-5

L1 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2007 ACS on STN
RN 781658-23-9 REGISTRY
ED Entered STN: 16 Nov 2004
CN L-Isoleucine, 4-hydroxy- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **4-Hydroxyisoleucine**
FS STEREOSEARCH
MF C6 H13 N O3
SR CA
LC STN Files: CA, CAPLUS, CHEMCATS, IMSDRUGNEWS, IMSRESEARCH, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry.

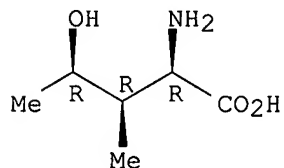


****PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT****

26 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
27 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2007 ACS on STN
RN 60010-78-8 REGISTRY
ED Entered STN: 16 Nov 1984
CN D-Xylonic acid, 2-amino-2,3,5-trideoxy-3-methyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **(2R,3R,4R)-4-Hydroxyisoleucine**
CN (4R)-4-Hydroxy-D-alloisoleucine
FS STEREOSEARCH
DR 50764-07-3
MF C6 H13 N O3
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, CHEMINFORMRX, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (-).

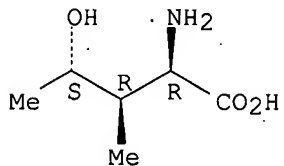


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9 REFERENCES IN FILE CA (1907 TO DATE)
9 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2007 ACS on STN
RN 60010-73-3 REGISTRY
ED Entered STN: 16 Nov 1984
CN L-Arabinonic acid, 2-amino-2,3,5-trideoxy-3-methyl- (CA INDEX NAME)
OTHER NAMES:
CN **(2R,3R,4S)-4-Hydroxyisoleucine**
CN (4S)-4-Hydroxy-D-alloisoleucine
FS STEREOSEARCH
MF C6 H13 N O3
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, CHEMINFORMRX, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (+).

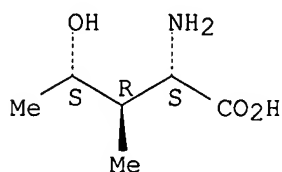


****PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT****

10 REFERENCES IN FILE CA (1907 TO DATE)
10 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2007 ACS on STN
 RN 55399-93-4 REGISTRY
 ED Entered STN: 16 Nov 1984
 CN L-Ribonic acid, 2-amino-2,3,5-trideoxy-3-methyl- (CA INDEX NAME)
 OTHER NAMES:
 CN **(2S,3R,4S)-4-Hydroxyisoleucine**
 CN (4S)-4-Hydroxy-L-isoleucine
 FS STEREOSEARCH
 MF C6 H13 N O3
 LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, CHEMINFORMRX, TOXCENTER,
 USPAT2, USPATFULL
 (*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (+).

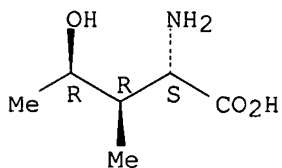


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31 REFERENCES IN FILE CA (1907 TO DATE)
 31 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2007 ACS on STN
 RN 55399-92-3 REGISTRY
 ED Entered STN: 16 Nov 1984
 CN D-Lyxonic acid, 2-amino-2,3,5-trideoxy-3-methyl- (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN Isoleucine, 4-hydroxy-, (2S,3R,4R)- (8CI)
 OTHER NAMES:
 CN **(2S,3R,4R)-4-Hydroxyisoleucine**
 CN (4R)-4-Hydroxy-L-isoleucine
 FS STEREOSEARCH
 DR 21704-86-9, 50764-06-2
 MF C6 H13 N O3
 LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX,
 CSCHEM, TOXCENTER, USPATFULL
 (*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

17 REFERENCES IN FILE CA (1907 TO DATE)
 17 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus medline biosis

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

20.10

20.31

FILE 'CAPLUS' ENTERED AT 16:58:06 ON 21 JUN 2007

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FILE 'MEDLINE' ENTERED AT 16:58:06 ON 21 JUN 2007

FILE 'BIOSIS' ENTERED AT 16:58:06 ON 21 JUN 2007

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=> s l1 or 4-hydroxyisoleucine or 4-hydroxy-L-isoleucine

L2 128 L1 OR 4-HYDROXYISOLEUCINE OR 4-HYDROXY-L-ISOLEUCINE

=> s l2 and (insulin or diabetes or insuline)

L3 59 L2 AND (INSULIN OR DIABETES OR INSULINE)

=> focus

PROCESSING COMPLETED FOR L3

L4 59 FOCUS L3 1-

=> s l4 and pd <=2000

2 FILES SEARCHED...

L5 18 L4 AND PD <=2000

=> s l4 and (hyperinsulinemia or (high (l) insulin) or hyperinsulinism)

L6 9 L4 AND (HYPERINSULINEMIA OR (HIGH (L) INSULIN) OR HYPERINSULINI
SM)

=> dup rem l6

PROCESSING COMPLETED FOR L6

L7 7 DUP REM L6 (2 DUPLICATES REMOVED)

=> s l5 dup rem

MISSING OPERATOR L5 DUP

The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> dup rem l5

PROCESSING COMPLETED FOR L5

L8 12 DUP REM L5 (6 DUPLICATES REMOVED)

=> d ibib abs 1-9 hitstr

L8 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:999654 CAPLUS

DOCUMENT NUMBER: 141:406105

TITLE: Methods and compositions using β -alanylhistidine
peptides and β -alanines for increasing the
anaerobic working capacity in tissues

INVENTOR(S): Harris, Roger; Dunnett, Mark

PATENT ASSIGNEE(S): Natural Alternatives International, UK

SOURCE: U.S. Pat. Appl. Publ., 33 pp., Cont.-in-part of U.S.
Ser. No. 209,169.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.

KIND

DATE

APPLICATION NO.

DATE

US 2004229773	A1	20041118	US 2003-717217	20031118
US 5965596	A	19991012	US 1997-909513	19970812 <--
US 6172098	B1	20010109	US 1999-318530	19990525
US 2001005579	A1	20010628	US 2001-757782	20010109
US 6426361	B2	20020730		
US 2003100513	A1	20030529	US 2002-209169	20020730
US 6680294	B2	20040120		
CA 2521987	A1	20041028	CA 2004-2521987	20040408
WO 2004091497	A2	20041028	WO 2004-US11050	20040408
WO 2004091497	A3	20050310		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1610800	A2	20060104	EP 2004-749952	20040408
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
JP 2006522821	T	20061005	JP 2006-509880	20040408

PRIORITY APPLN. INFO.:

GB 1996-16910	A	19960812
GB 1996-21914	A	19961021
US 1997-909513	A3	19970812
US 1999-318530	A1	19990525
US 2001-757782	A1	20010109
US 2002-209169	A2	20020730
US 2003-462238P	P	20030410
US 2003-717217	A	20031118
WO 2004-US11050	W	20040408

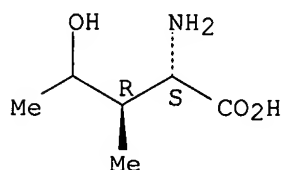
AB The invention provides compns. comprising β -alanylhistidine peptides and β -alanines, and methods for administering these peptides and amino acids. In one aspect, the compns. and methods cause an increase in the blood plasma concns. of β alanine and/or creatine.

IT **781658-23-9**
 RL: BUU (Biological use, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (β -alanylhistidine peptides and β -alanines for increasing anaerobic working capacity in tissues)

RN 781658-23-9 CAPLUS

CN L-Isoleucine, 4-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1
 ACCESSION NUMBER: 2000:156040 CAPLUS
 DOCUMENT NUMBER: 132:317627
 TITLE: **4-Hydroxyisoleucine:** effects of synthetic and natural analogues on insulin secretion

AUTHOR(S): Broca, C.; Manteghetti, M.; Gross, R.; Baissac, Y.;
Jacob, M.; Petit, P.; Sauvaire, Y.; Ribes, G.
CORPORATE SOURCE: UMR 9921 du Centre National de la Recherche
Scientifique, Montpellier, Fr.
SOURCE: European Journal of Pharmacology (2000),
390(3), 339-345
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

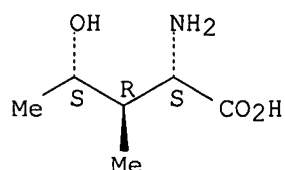
AB **4-Hydroxyisoleucine**, a peculiar amino acid extracted from
fenugreek seeds and never found in mammalian tissues, exhibits interesting
insulinotropic activity. To investigate the structural requirements for
this stimulating effect, the insulinotropic activity of the major isomer
(2S,3R,4S) of **4-hydroxyisoleucine**, in the presence of
8.3 mM glucose, was compared to that of its minor isomer (2R,3R,4S), its
lactone form, classical structurally related amino acids, and synthetic
monomethylated analogs. In the isolated, ex vivo, perfused rat pancreas,
only the major isomer of **4-hydroxyisoleucine** (200
μM) potentiated **insulin** release. On incubated isolated rat
islets, the threshold concentration for a significant increase (P<0.05) in
insulin release was 200 μM for (2S,3R,4S) **4-**
hydroxyisoleucine, 500 μM for (2S,4R) and (2S,4S)
γ-hydroxynorvalines as well as (2S,3S) and (2S,3R)
γ-hydroxyvalines, and 1 mM or more for other congeners. In
conclusion, the insulinotropic properties of **4-**
hydroxyisoleucine, in the micromolar range, are seen only in the
presence of the linear major isoform; they also require carbon α in
S-configuration, full methylation and carbon γ-hydroxylation.

IT **55399-93-4, (2S,3R,4S)-4-Hydroxyisoleucine**
60010-73-3, (2R,3R,4S)-4-Hydroxyisoleucine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); PRP (Properties); BIOL (Biological study)
(structural requirements for insulinotropic effect of **4-**
Hydroxyisoleucine in isolated rat pancreas)

RN 55399-93-4 CAPLUS

CN L-Ribonic acid, 2-amino-2,3,5-trideoxy-3-methyl- (CA INDEX NAME)

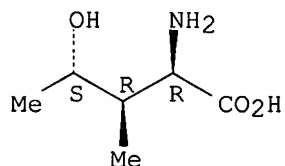
Absolute stereochemistry. Rotation (+).



RN 60010-73-3 CAPLUS

CN L-Arabinonic acid, 2-amino-2,3,5-trideoxy-3-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT:

17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 1999:714049 CAPLUS

DOCUMENT NUMBER: 132:44784

TITLE: **4-Hydroxyisoleucine**: experimental evidence of its insulinotropic and antidiabetic properties

AUTHOR(S): Broca, Christophe; Gross, Rene; Petit, Pierre; Sauvaire, Yves; Manteghetti, Michele; Tournier, Michel; Masiello, Pellegrino; Gomis, Ramon; Ribes, Gerard

CORPORATE SOURCE: Unite Mixte de Recherche 9921 du Centre National de la Recherche Scientifique, and Faculte de Medecine and Laboratoire de Recherche sur les Substances Naturelles Vegetales, UPRES EA 1677, Laboratoire de Pharmacologie, Montpellier, 34060, Fr.

SOURCE: American Journal of Physiology (1999), 277(4, Pt. 1), E617-E623

CODEN: AJPHAP; ISSN: 0002-9513

PUBLISHER: American Physiological Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have recently shown in vitro that **4-hydroxyisoleucine** (4-OH-Ile), an amino acid extracted from fenugreek seeds, potentiates **insulin** secretion in a glucose-dependent manner. The present study was designed to investigate whether 4-OH-Ile could exert in vivo insulinotropic and antidiabetic properties. For this purpose, i.v. or oral glucose tolerance tests (IVGTTs and OGTTs, resp.) were performed not only in normal animals but also in a type II **diabetes** rat model. During IVGTT in normal rats or OGTT in normal dogs, 4-OH-Ile (18 mg/kg) improved glucose tolerance. The lactonic form of 4-OH-Ile was ineffective in normal rats. In non-**insulin**-dependent diabetic (NIDD) rats, a single i.v. administration of 4-OH-Ile (50 mg/kg) partially restored glucose-induced **insulin** response without affecting glucose tolerance; a 6-day subchronic administration of 4-OH-Ile (50 mg/kg, daily) reduced basal hyperglycemia, decreased basal insulinemia, and slightly, but significantly, improved glucose tolerance. In vitro, 4-OH-Ile (200 μ M) potentiated glucose (16.7 mM)-induced **insulin** release from NIDD rat-isolated islets. So, the antidiabetic effects of 4-OH-Ile on NIDD rats result, at least in part, from a direct pancreatic B cell stimulation.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:507230 CAPLUS

DOCUMENT NUMBER: 129:269766

TITLE: Antidiabetic and hypocholesterolemic effects of fenugreek

AUTHOR(S): Al-Habbori, Molham; Raman, Amala

CORPORATE SOURCE: Department of Clinical Biochemistry, Faculty of Medicine and Health Sciences, University of Sana'a, Sana'a, Yemen

SOURCE: Phytotherapy Research (1998), 12(4), 233-242

CODEN: PHYREH; ISSN: 0951-418X

PUBLISHER: John Wiley & Sons Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with many refs. The seeds of *Trigonella foenum graecum* (fenugreek) have been reported to have antidiabetic and hypocholesterolemic properties in both animal models and humans. Activity has been attributed largely to fenugreek's saponin and high fiber content, and is probably not related to its major alkaloid trigonelline. Antihyperglycemic effects have been linked to delayed gastric emptying caused by the fiber content, and to (unidentified) components that inhibit

carbohydrate digestive enzymes. Fenugreek administration may increase plasma **insulin** levels in vivo. Its major free amino acid, **4-hydroxyisoleucine**, stimulates **insulin** secretion from perfused pancreas in vitro. The hypocholesterolemic effect has been attributed to increased conversion of hepatic cholesterol to bile salts due to loss, in the feces, of complexes of these substances with fenugreek fiber and saponins. Fenugreek treatment selectively reduces the LDL and VLDL fractions of total cholesterol, and HDL-cholesterol has also been reported to increase in alloxan-induced diabetic rats and type II diabetic individuals following treatment with fenugreek. Fenugreek administration has not been reported to cause any toxicol. effects. Its regular consumption may therefore be beneficial in the management of **diabetes** and the prevention of atherosclerosis and coronary heart disease.

REFERENCE COUNT: 129 THERE ARE 129 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 1998:70710 CAPLUS

DOCUMENT NUMBER: 128:200858

TITLE: **4-Hydroxyisoleucine**: a novel amino acid potentiator of **insulin** secretion

AUTHOR(S): Sauvaire, Yves; Petit, Pierre; Broca, Christophe; Manteghetti, Michele; Baissac, Yves;

Fernandez-Alvarez, Josepha; Gross, Rene; Roye, Michele; Leconte, Agnes; Gomis, Ramon; Ribes, Gerard
CORPORATE SOURCE: Laboratoire de Recherche sur les Substances Naturelles Vegetales, Unite Propre de Recherche Enseignement Superieur EA 1677, Universite Montpellier II, Montpellier, 34095, Fr.

SOURCE: Diabetes (1998), 47(2), 206-210
CODEN: DIAEAB; ISSN: 0012-1797

PUBLISHER: American Diabetes Association

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors report the characterization of a new insulinotropic compound, **4-hydroxyisoleucine**. This amino acid has been extracted and purified from fenugreek seeds, which are known in traditional medicine for their antidiabetic properties. **4-Hydroxyisoleucine** increases glucose-induced **insulin** release, in the concentration range of 100 μ M to 1 mM, through a direct effect on isolated islets of Langerhans from both rats and humans. The stimulating effect of **4-hydroxyisoleucine** was strictly glucose dependent; indeed, ineffective at low (3 mM) or basal (5 mM) glucose concns., the amino acid potentiated the **insulin** secretion induced by supranormal (6.6-16.7 mM) concns. of glucose. In addition, in the isolated perfused rat pancreas, the authors could show (1) that the pattern of **insulin** secretion induced by **4-hydroxyisoleucine** was biphasic, (2) that this effect occurred in the absence of any change in pancreatic α - and δ -cell activity, and (3) that the more glucose concentration was increased, the more **insulin** response was amplified. Moreover, **4-hydroxyisoleucine** did not interact with other agonists of **insulin** secretion (leucine, arginine, tolbutamide, glyceraldehyde). Therefore, the authors conclude that **4-hydroxyisoleucine** insulinotropic activity might, at least in part, account for fenugreek seeds' antidiabetic properties. This secretagogue may be considered as a novel drug with potential interest for the treatment of NIDDM.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:617969 CAPLUS

DOCUMENT NUMBER: 127:257635
 TITLE: Antidiabetic composition containing (2S, 3R, 4S)-
4-hydroxyisoleucine
 INVENTOR(S): Sauvaire, Yves; Ribes, Gerard
 PATENT ASSIGNEE(S): Societe Civile de Gestion Jouvenet, Fr.; Sauvaire,
 Yves; Ribes, Gerard
 SOURCE: PCT Int. Appl., 25 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9732577	A1	19970912	WO 1997-FR420	19970307 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2745718	A1	19970912	FR 1996-2955	19960308 <--
FR 2745718	B1	19980507		
AU 9720319	A	19970922	AU 1997-20319	19970307 <--
PRIORITY APPLN. INFO.:			FR 1996-2955	A 19960308
			WO 1997-FR420	W 19970307

AB An antidiabetic composition capable of stimulating **insulin** secretion and particularly suitable for treating non-**insulin**-dependent **diabetes** is disclosed. The composition contains (2S, 3R, 4S)-4-**hydroxyisoleucine**, and/or the lactone form thereof, and is substantially free of any other stereoisomer of this compound

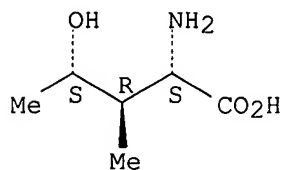
IT **55399-93-4P**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(hydroxyisoleucine isomer antidiabetic composition)

RN 55399-93-4 CAPLUS

CN L-Ribonic acid, 2-amino-2,3,5-trideoxy-3-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **60010-73-3P**

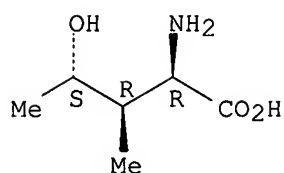
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)

(hydroxyisoleucine isomer antidiabetic composition)

RN 60010-73-3 CAPLUS

CN L-Arabinonic acid, 2-amino-2,3,5-trideoxy-3-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L8 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 4
 ACCESSION NUMBER: 1997:116899 CAPLUS
 DOCUMENT NUMBER: 126:247872
 TITLE: Characterization of a dioxygenase from *Trigonella foenum-graecum* involved in 4-hydroxyisoleucine biosynthesis
 AUTHOR(S): Haefele, Catherine; Bonfils, Claude; Sauvaire, Yves
 CORPORATE SOURCE: Lab. Rech. Substances Naturelles Vegetales, Univ. Montpellier II, Montpellier, 30495, Fr.
 SOURCE: Phytochemistry (1997), 44(4), 563-566
 CODEN: PYTCAS; ISSN: 0031-9422
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English

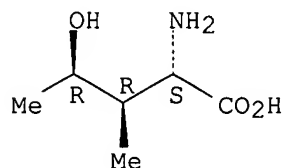
AB **4-Hydroxyisoleucine**, an unusual amino acid known for its **insulin**-stimulating effect, was detected by HPLC following isoleucine incubation with a cell-free extract from etiolated 6-day-old fenugreek seedlings in the presence of various cofactors. The reaction showed that **4-hydroxyisoleucine** formation is dependent on the presence of Fe²⁺, 2-oxoglutarate, ascorbate and oxygen. This suggests that a 2-oxoacid-dependent dioxygenase plays a key role in this biosynthetic pathway.

IT **55399-92-3**
 RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
 (formation of **insulin**-stimulating amino acid by fenugreek cell-free extract)

RN 55399-92-3 CAPLUS

CN D-Lyxonic acid, 2-amino-2,3,5-trideoxy-3-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 8 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 ACCESSION NUMBER: 1997:370719 BIOSIS
 DOCUMENT NUMBER: PREV199799669922
 TITLE: Calcium signalling is involved in the **insulin**-releasing effect of **4-hydroxyisoleucine**
 AUTHOR(S): Petit, P. [Reprint author]; Liu, Y. J.; Broca, C. [Reprint author]; Sauvaire, Y.; Ribes, G. [Reprint author]; Gylfe, E.
 CORPORATE SOURCE: Lab. Pharmacol., Fac. Med., Univ. Montpellier, II Montpellier, France
 SOURCE: Diabetologia, (1997) Vol. 40, No. SUPPL. 1, pp. A112.
 Meeting Info.: 16th International Diabetes Federation

Congress. Helsinki, Finland. July 20-25, 1997.
 CODEN: DBTGAJ. ISSN: 0012-186X.

DOCUMENT TYPE: Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)
 Conference; (Meeting Poster)

LANGUAGE: English

ENTRY DATE: Entered STN: 4 Sep 1997
 Last Updated on STN: 4 Sep 1997

L8 ANSWER 9 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1996:452132 BIOSIS

DOCUMENT NUMBER: PREV199699174488

TITLE: Could **4-hydroxyisoleucine** be used as a
 hypoglycaemic agent in the treatment of type 2
diabetes mellitus?.

AUTHOR(S): Fernandez-Alvarez, J. [Reprint author]; Sauvaire, Y.;
 Petit, P.; Casamitjana, R.; Ribes, G.; Gomis, R.

CORPORATE SOURCE: Endocrinol. Unit/Hormonal Lab., Hosp. Clinic, Barcelona,
 Spain

SOURCE: Diabetologia, (1996) Vol. 39, No. SUPPL. 1, pp.
 A234.
 Meeting Info.: 32nd Annual Meeting of the European
 Association for the Study of Diabetes. Vienna, Austria.
 September 1-5, 1996.
 CODEN: DBTGAJ. ISSN: 0012-186X.

DOCUMENT TYPE: Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)
 Conference; (Meeting Poster)

LANGUAGE: English

ENTRY DATE: Entered STN: 7 Oct 1996
 Last Updated on STN: 7 Oct 1996

=> d ibib abs hitstr 10-12

L8 ANSWER 10 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
 STN

ACCESSION NUMBER: 1996:452133 BIOSIS

DOCUMENT NUMBER: PREV199699174489

TITLE: Structure activity analysis of different analogues of the
 new insulintropic agent **4-**
hydroxyisoleucine.

AUTHOR(S): Ribes, G. [Reprint author]; Broca, C.; Petit, P.; Jacob,
 M.; Baissac, Y.; Manteghetti, M.; Roye, M.; Sauvaire, Y.

CORPORATE SOURCE: Fac. Med., UMR 9921 CNRS, Univ. Montpellier II, France

SOURCE: Diabetologia, (1996) Vol. 39, No. SUPPL. 1, pp.
 A234.
 Meeting Info.: 32nd Annual Meeting of the European
 Association for the Study of Diabetes. Vienna, Austria.
 September 1-5, 1996.
 CODEN: DBTGAJ. ISSN: 0012-186X.

DOCUMENT TYPE: Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)
 Conference; (Meeting Poster)

LANGUAGE: English

ENTRY DATE: Entered STN: 7 Oct 1996
 Last Updated on STN: 7 Oct 1996

L8 ANSWER 11 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
 STN

ACCESSION NUMBER: 1995:425001 BIOSIS

DOCUMENT NUMBER: PREV199598439301

TITLE: **Insulin** stimulating effect of an original amino
 acid, **4-hydroxyisoleucine**, purified

from fenugreek seeds.

AUTHOR(S): Petit, P.; Sauvaire, Y.; Hillaire-Buys, D.; Manteghetti, M.; Baissac, Y.; Gross, R.; Ribes, G.

CORPORATE SOURCE: Lab. Pharmacol., Fac. Med., UMR 9921 CNRS, Lab. Recherche Substances Naturelles Vegetales, Montpellier, France

SOURCE: Diabetologia, (1995) Vol. 38, No. SUPPL. 1, pp. A101.
Meeting Info.: 31st Annual Meeting of the European Association for the Study of Diabetes. Stockholm, Sweden. September 12-16, 1995.
CODEN: DBTGJ. ISSN: 0012-186X.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)

LANGUAGE: English

ENTRY DATE: Entered STN: 3 Oct 1995
Last Updated on STN: 3 Oct 1995

L8 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1994:280270 CAPLUS

DOCUMENT NUMBER: 120:280270

TITLE: Pharmaceutical compositions containing mono or polyhydroxylated amino acids for the treatment of non-insulin dependent diabetes mellitus

INVENTOR(S): Sauvaire, Yves; Ribes, Gerard

PATENT ASSIGNEE(S): Laboratoires Monal, Fr.

SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 587476	A1	19940316	EP 1993-402135	19930901 <--
EP 587476	B1	19980318		
R: AT, BE, CH, DE, DK, ES, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
FR 2695317	A1	19940311	FR 1992-10644	19920907 <--
FR 2695317	B1	19950310		
JP 06157302	A	19940603	JP 1993-217588	19930901 <--
AT 164064	T	19980415	AT 1993-402135	19930901 <--
ES 2116421	T3	19980716	ES 1993-402135	19930901 <--
CA 2105502	A1	19940308	CA 1993-2105502	19930903 <--
CA 2105502	C	20001121		
IN 183194	A1	19991002	IN 1994-DE244	19940301 <--
PRIORITY APPLN. INFO.:			FR 1992-10644	A 19920907

AB The title amino acids are extracted from plants and are used as antidiabetic agents. Thus, **4-hydroxyisoleucine** was extracted from fenugreek seeds (preparation given) and used at 500µM on isolated rat pancreas in presence of 8.3mM glucose for 10min. The amount of **insulin** secreted was 2206 as compared to 810µM.

=> d ibib abs hitstr 1-7 17

L7 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2005:146900 CAPLUS

DOCUMENT NUMBER: 142:410368

TITLE: The addition of fenugreek extract (Trigonella foenum-graecum) to glucose feeding increases muscle glycogen resynthesis after exercise

AUTHOR(S): Ruby, B. C.; Gaskill, S. E.; Slivka, D.; Harger, S. G.

CORPORATE SOURCE: Department of Health and Human Performance, The

SOURCE: University of Montana, Missoula, MT, USA
Amino Acids (2005), 28(1), 71-76
CODEN: AACIE6; ISSN: 0939-4451
PUBLISHER: Springer Wien
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The purpose of this study was to determine the effects of ingesting an oral supplement containing **4-Hydroxyisoleucine** (4-OH-Ile, isolated from fenugreek seeds [*Trigonella foenum-graecum*]) with a glucose beverage on rates of post-exercise muscle glycogen resynthesis in trained male cyclists. Following an overnight fast (12 h), subjects completed a 90-min glycogen depletion ride after which a muscle biopsy was obtained from the vastus lateralis. Immediately and 2 h after the muscle biopsy, subjects ingested either an oral dose of dextrose (Glu) (1.8 g·kg BW-1) or 4-OH-Ile supplement (Glu + 4-OH-Ile, including 2.0 mg·kg-1 4-OH-Ile with the same oral dose of dextrose) with a second muscle biopsy 4 h after exercise. Post exercise muscle glycogen concentration was similar

for both trials. Overall, there was a significant increase in glucose and **insulin** concns. from time 0 throughout the majority of the 4-h recovery period, with no significant differences between the two trials at any time point. Although muscle glycogen concentration significantly increased from immediately post exercise to 4 h of recovery for both trials, the net rate of muscle glycogen resynthesis was 63 greater during Glu + 4-OH-Ile (10.6±3.3 vs. 6.5±2.6 g·kg wet weight-1·hr.-1 for the Glu + 4-OH-Ile and Glu trials, resp.). These data demonstrate that when the fenugreek extract supplement (4-OH-Ile) is added to a **high** oral dose of dextrose, rates of post-exercise glycogen resynthesis are enhanced above dextrose alone.

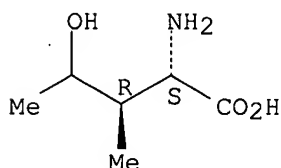
IT 781658-23-9

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(the addition of fenugreek extract (*Trigonella foenum-graecum*) to glucose feeding increases muscle glycogen resynthesis after exercise)

RN 781658-23-9 CAPLUS

CN L-Isoleucine, 4-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 7

MEDLINE on STN

ACCESSION NUMBER: 2004404025 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15082420

TITLE: Insulinotropic agent ID-1101 (4-hydroxyisoleucine) activates insulin signaling in rat.

AUTHOR: Broca Christophe; Breil Vincent; Cruciani-Guglielmacci Celine; Manteghetti Michele; Rouault Christine; Derouet Michel; Rizkalla Salwa; Pau Bernard; Petit Pierre; Ribes Gerard; Ktorza Alain; Gross Rene; Reach Gerard; Taouis Mohammed

CORPORATE SOURCE: Laboratoire de Pharmacologie, Centre de Pharmacologie et Biotechnologies pour la Sante-Unité Mixte de Recherche 5160 Centre National de la Recherche Scientifique, Faculté de Médecine, 34060 Montpellier, France.. christophe.broca@univ-

montpl.fr

SOURCE: American journal of physiology. Endocrinology and metabolism, (2004 Sep) Vol. 287, No. 3, pp. E463-71.
Electronic Publication: 2004-04-13.
Journal code: 100901226. ISSN: 0193-1849.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200409

ENTRY DATE: Entered STN: 14 Aug 2004
Last Updated on STN: 11 Sep 2004
Entered Medline: 10 Sep 2004

AB ID-1101 (**4-hydroxyisoleucine**), an amino acid extracted from fenugreek seeds, exhibits an interesting glucose-dependent **insulin**-stimulating activity. The present study was undertaken to investigate a possible extrapancreatic effect of ID-1101 on **insulin** signaling and action besides its previously described insulinotropic action. **Insulin**-sensitizing effects of ID-1101 were investigated in rat in vivo by three different approaches: 1) using euglycemic hyperinsulinemic clamps in two different rat models of **insulin** resistance, i.e., Zucker fa/fa rats and rats fed a sucrose-lipid diet; 2) measuring liver and muscle phosphatidylinositol (PI) 3-kinase activity after an acute injection of ID-1101 in normal and **insulin**-resistant diabetic rats; and 3) after chronic treatment in two rat models of **insulin** resistance. Euglycemic hyperinsulinemic clamp experiments revealed that ID-1101 can improve **insulin** resistance through an increase of peripheral glucose utilization rate in sucrose-lipid-fed rats and by decreasing hepatic glucose production in Zucker fa/fa rats. Moreover, we demonstrated that a single injection of ID-1101 activates the PI 3-kinase activity in liver and muscle from normal rats but also in muscle from diabetic rats. Finally, chronic ID-1101 treatment significantly reduced insulinemia in type 2 diabetic rats and reduced the progression of **hyperinsulinemia** in **insulin**-resistant obese Zucker fa/fa rats. These findings clearly demonstrate that ID-1101 can reduce **insulin** resistance through activation of the early steps of **insulin** signaling in peripheral tissues and in liver. In summary, ID-1101, besides its insulinotropic effect, directly improves **insulin** sensitivity, making it a potentially very valuable therapeutic agent for **diabetes** treatment.

L7 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:435594 CAPLUS

TITLE: Exploring Synthetic Routes to 4-Hydroxyamino Acids: Potential Blood Glucose Regulating Agents

AUTHOR(S): Davies, Don R.; Vellinga, Jonathan

CORPORATE SOURCE: Chemistry, Weber State University, Ogden, UT, 84408, USA

SOURCE: Abstracts, Joint Regional Meeting of the Northwest and Rocky Mountain Sections of the American Chemical Society, Logan, UT, United States, June 6-9 (2004), GEN-140. American Chemical Society: Washington, D. C. CODEN: 69FLZI

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB **4-Hydroxyisoleucine**, a rare amino acid found only in few plant sources, has been found to possess potent **insulin** releasing activity in the presence of moderate to **high** blood glucose concns., and therefore, may be used in the treatment of hyperglycemia. Since **4-hydroxyisoleucine** is difficult to isolate from plant sources we wish to synthetically produce it on a larger scale in our labs. Addnl., a synthetic approach provides

flexibility to producing other 4-hydroxyamino acids that may have improved properties over **4-hydroxyisoleucine**. In our presentation we will discuss and compare possible synthetic routes leading to 4-hydroxyamino acids. We will also address what we have accomplished toward the synthesis of these rare aminoacids and what we hope to accomplish in the near future.

L7 ANSWER 4 OF 7 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 ACCESSION NUMBER: 2004:13813 BIOSIS
 DOCUMENT NUMBER: PREV200400013001
 TITLE: The insulinotropic agent **4-hydroxyisoleucine** also activates insulin signaling in vivo and in vitro.
 AUTHOR(S): Broca, C. [Reprint Author]; Breil, V.; Manteghetti, M. [Reprint Author]; Derouet, M.; Petit, P. [Reprint Author]; Ribes, G. [Reprint Author]; Gross, R. [Reprint Author]; Reach, G.; Taouis, M.
 CORPORATE SOURCE: Laboratoire de Pharmacologie du Diabete, CNRS UMR 5094, Montpellier, France
 SOURCE: Diabetes & Metabolism, (August 2003) Vol. 29, No. Hors serie 2, pp. 4S96. print.
 Meeting Info.: 18th International Diabetes Federation Congress. Paris, France. August 24-29, 2003.
 ISSN: 1262-3636.
 DOCUMENT TYPE: Conference; (Meeting)
 Conference; (Meeting Poster)
 Conference; Abstract; (Meeting Abstract)
 LANGUAGE: English
 ENTRY DATE: Entered STN: 24 Dec 2003
 Last Updated on STN: 24 Dec 2003

L7 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2001:167800 CAPLUS
 DOCUMENT NUMBER: 134:202704
 TITLE: Use of amino acids for making medicines for treating **insulin-resistance**
 INVENTOR(S): Ribes, Gerard; Taouis, Mohammed; Petit, Pierre Roger; Broca, Christophe; Sauvaire, Yves; Pau, Bernard
 PATENT ASSIGNEE(S): Centre National de la Recherche Scientifique (CNRS), Fr.; Institut National de la Recherche Agronomique (INRA)
 SOURCE: PCT Int. Appl., 37 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001015689	A1	20010308	WO 2000-FR2361	20000823
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2797767	A1	20010302	FR 1999-10874	19990827
FR 2797767	B1	20020614		
CA 2382835	A1	20010308	CA 2000-2382835	20000823
EP 1206257	A1	20020522	EP 2000-958726	20000823

EP 1206257 B1 20041103
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL
 JP 2003508435 T 20030304 JP 2001-519903 20000823
 EP 1421937 A1 20040526 EP 2003-291523 20000823
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI, CY
 AT 281159 T 20041115 AT 2000-958726 20000823
 PT 1206257 T 20050331 PT 2000-958726 20000823
 ES 2231247 T3 20050516 ES 2000-958726 20000823
 ZA 2002001619 A 20030526 ZA 2002-1619 20020226
 HK 1052456 A1 20051028 HK 2002-108489 20021122
 PRIORITY APPLN. INFO.: FR 1999-10874 A 19990827
 EP 2000-958726 A3 20000823
 WO 2000-FR2361 W 20000823

AB The invention concerns the use of monohydroxy or polyhydroxy amino acids, and the lactone forms thereof for making medicines with **insulin** -analog and/or **insulin**-sensitizing effects on peripheral tissues targeted by **insulin**, and more particularly the use thereof for making medicines for treating and preventing **insulin**-resistance. Injection of 200 µg/kg 4-hydroxy isoleucine i.p. induced the activation of **insulin** receptor and **insulin** receptor substrate-1 which was comparable to **insulin** injection.

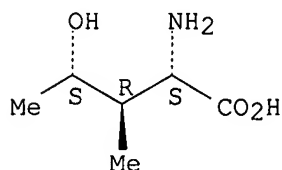
IT **55399-93-4**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of amino acids for making medicines for treating **insulin** -resistance)

RN 55399-93-4 CAPLUS

CN L-Ribonic acid, 2-amino-2,3,5-trideoxy-3-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L7 ANSWER 6 OF 7 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 ACCESSION NUMBER: 2002:594815 BIOSIS
 DOCUMENT NUMBER: PREV200200594815
 TITLE: Effect of **4-hydroxyisoleucine** on **insulin** sensitivity in **insulin** resistant rats.
 AUTHOR(S): Breil, V. [Reprint author]; Rouault, C. [Reprint author]; Rizkalla, S. [Reprint author]; Broca, C.; Taouis, M.; Petit, P.; Reach, G. [Reprint author]
 CORPORATE SOURCE: Service de Diabetologie, INSERM U341, Hotel-Dieu, Paris, France
 SOURCE: Diabetologia, (August, 2001) Vol. 44, No. Supplement 1, pp. A 79. print.
 Meeting Info.: 37th Annual Meeting of the European Association for the Study of Diabetes. Glasgow, Scotland, UK. September 09-13, 2001. European Association for the Study of Diabetes.
 CODEN: DBTGAI. ISSN: 0012-186X.
 DOCUMENT TYPE: Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)
 LANGUAGE: English

ENTRY DATE: Entered STN: 20 Nov 2002
Last Updated on STN: 20 Nov 2002

L7 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:507230 CAPLUS
DOCUMENT NUMBER: 129:269766
TITLE: Antidiabetic and hypocholesterolemic effects of
fenugreek
AUTHOR(S): Al-Habbori, Molham; Raman, Amala
CORPORATE SOURCE: Department of Clinical Biochemistry, Faculty of
Medicine and Health Sciences, University of Sana'a,
Sana'a, Yemen
SOURCE: Phytotherapy Research (1998), 12(4), 233-242
CODEN: PHYREH; ISSN: 0951-418X
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with many refs. The seeds of *Trigonella foenum graecum* (fenugreek) have been reported to have antidiabetic and hypocholesterolemic properties in both animal models and humans. Activity has been attributed largely to fenugreek's saponin and **high** fiber content, and is probably not related to its major alkaloid trigonelline. Antihyperglycemic effects have been linked to delayed gastric emptying caused by the fiber content, and to (unidentified) components that inhibit carbohydrate digestive enzymes. Fenugreek administration may increase plasma **insulin** levels in vivo. Its major free amino acid, **4-hydroxyisoleucine**, stimulates **insulin** secretion from perfused pancreas in vitro. The hypocholesterolemic effect has been attributed to increased conversion of hepatic cholesterol to bile salts due to loss, in the feces, of complexes of these substances with fenugreek fiber and saponins. Fenugreek treatment selectively reduces the LDL and VLDL fractions of total cholesterol, and HDL-cholesterol has also been reported to increase in alloxan-induced diabetic rats and type II diabetic individuals following treatment with fenugreek. Fenugreek administration has not been reported to cause any toxicol. effects. Its regular consumption may therefore be beneficial in the management of **diabetes** and the prevention of atherosclerosis and coronary heart disease.

REFERENCE COUNT: 129 THERE ARE 129 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT